REMARKS

The Amendments to the Claims

Claim 1 has been amended by replacing the phrase "the prodrugs thereof, and the pharmaceutically acceptable salts of the compounds and prodrugs," with the phrase "or a pharmaceutically acceptable salt thereof." Also, the numbering of the groups in the definition of the variables R^1 and R^2 was amended to (i) through (vii) from the previous (ii) through (viii) to correct that typographical error. Support for these amendment is in the specification as originally filed, including original claim 1.

In claims 2-5 the term "prodrugs" has been deleted from the claims and in claims 2-3 the pharmaceutically acceptable salt thereof language was added.

In claim 4 the compound name "5-[2-(6-*tert*-butyl-3-oxo-2,3-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-8-ylamino)-nicotinic acid methyl ester;" was deleted and was replaced with the correct compound name "5-[2-(6-*tert*-Butyl-3-oxo-2,3-dihydro-[1,2,4]triazolo[4,3-a]pyrazin-8-ylamino)-ethoxy]-nicotinic acid methyl ester." Support for this amendment is in the specification as originally filed, particularly at Example 96.

New dependent claim 13 has been added. Support for this claim is in the specification as originally file, including original claim 7.

No new matter is added by these amendments. Applicants respectfully request entry of the foregoing amendments.

The Objection to the Oath/Declaration

The Examiner has object to the oath/declaration as it allegedly does not provide the addresses of the inventors. Applicants respectfully submit that all required information is present in the Application Data Sheet submitted June 2009. Applicants respectfully request the Examiner to withdraw this objection.

The claim objections

The Examiner has objected to claim 1 as not being in proper alternative format. Applicants respectfully submit that the claims, as amended, are in proper alternative format. In view of this Applicants respectfully request the Examiner to withdraw this objection.

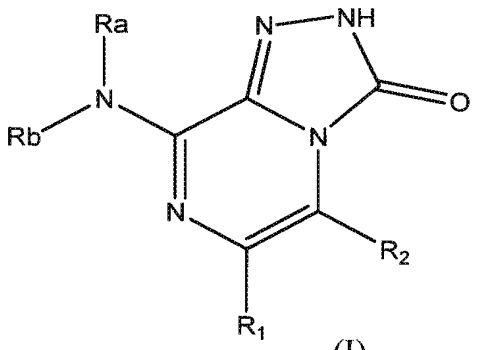
The 35 U.S.C.§112, first paragraph rejection

Claims 1-5 have been rejected under 35 U.S.C.§112, first paragraph as allegedly not being enabled. The Examiner has stated that the claims are enabled for triazolopyrazines where R^1 and R^2 are hydrogen or alkyl but not other R groups or for prodrugs of the compounds of formula I. Applicants traverse with respect to the alleged lack of enablement of compounds of formula I in which R^1 and R^2 are other than hydrogen or alkyl. The term "prodrug" has been deleted from the claims with the instant amendment and thus the 35 U.S.C.§112, first paragraph rejection based on that term is rendered moot.

An applicant's specification must enable a person skilled in the art to make and use the claimed invention without undue experimentation. The fact that experimentation is complex, however, will not make it undue if a person of skill in the art typically engages in such complex experimentation. See MPEP § 2164 *et. seq.*. for detailed guidance with regard to the enablement requirement of 35 U.S.C. § 112, first paragraph . There are many factors to be considered when determining whether a disclosure satisfies the enablement requirement. These factors include the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples and the quantity of experimentation required to make or use the invention based upon the disclosure. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

The Breadth of Claims 1-5

The breadth of claims 1-5, as amended, are directed to a specific genus of 8-amino-2H-[1,2,4]-triazolo[4,3-a]pyrazine-3-one derivatives of Formula (I) or a pharmaceutical composition thereof as shown below.



(I)

The definition of the variables R^a, R^b, R^1 and R^2 are as set forth in the claims.

The Nature of the Invention

The nature of the invention is a glycogen synthase kinase 3 inhibitor compound of formula I as set forth above, a pharmaceutical composition comprising them and a method of treating the specified glycogen kinase-3 mediated disorders with them.

The State of the Prior Art

The state of organic and medicinal chemistry is such that one of ordinary skill in the art would readily be able to make and use the compounds of Formula I in view of the teaching provided in the instant specification. Also, the nexus between glycogen synthase kinase 3 inhibition and the treatment of the specified diseases or disorders is known in the art.

The Predictability/Unpredictability of the Art and Level of Skill in the Art

Applicants respectfully submit that the instant disclosure provides enablement for one skilled in organic/medicinal to prepare the compounds of Formula I in a predictable manner. Thus, glycogen synthase kinase inhibitor compounds with appropriate pharmacological and pharmacodynamic properties can be prepared and used in methods of treating the specified diseases and disorders.

The Amount of Direction or Guidance and the Presence or Absence of Working Examples

Applicants have provided an extensive description of how to prepare the compounds of Formula I as described at page 18, line 23 through page 24, also Shemes 1-7 and Examples 1-237 at page 25-60 of the specification. Pharmaceutical compositions are described at page 16, line 19 through page 18, line 22 of the specification and methods of treatment are described at page 15, line 19 through page 16, line 18 of the specification. Biological assays describing the GSK inhibitory activity of the compounds are provided at page 60 through 62 of the specification. Thus, Applicants have provided extensive direction and guidance based on the specification in how to make and use the GSK inhibitor compounds of Formula I as instantly claimed.

The Examiner has stated that the compounds of Formula I are enabled when R^1 and R^2 are hydrogen or alkyl but that other R groups have not been taught. Applicants respectfully disagree with this statement. Compounds of Formula I wherein R^1 and R^2 are other than hydrogen and alkyl have been taught in the specification. Applicants respectfully request the Examiner to reconsider the specification with respect to the definition of R1 and R2, particularly the Examples. Applicants respectfully submit that compounds wherein R1 and/or R2 are other than hydrogen or alkyl have been taught. Examples 20-27, 45-47, 51-55, 63 and 65-66 provide compounds in which R1 and/or R2 is optionally substituted aryl. Examples 42 and 43 provide compounds in which R1 and/or R2 is alkyl with amide linked aryl. Examples 48-49 provide compounds where R1 and/or R2 is optionally substituted cycloalkyl. Example 56 provides a compound in which R1 and/or R2 is carboxy. Examples 57-62 provide compounds in which R1 and/or R2 is substituted amido. Example 118 provides a compound in which R1 and/or R2 is alkenyl. Applicants respectfully submit that numerous compounds with various substituents other than hydrogen and alkyl have been taught and specifically exemplified.

Issues also often arise about how much disclosure is necessary to teach one skilled in the art how to use a pharmaceutical compound in a method of treatment. In the case of In re Brana, 51 F.3d 1560, 34 U.S.P.Q.2d 1436 (Fed. Cir. 1995), the CAFC reversed a decision of the U.S. Board of Patent Appeals affirming an examiner's rejection of claims directed to 5-nitrobenzo[de]isoquinoline-1,3-dione compounds for use as antitumor

agents under 35 U.S.C. § 112 paragraph 1. The examiner's initial rejection, upon which the Board relied in rendering its decision, was based specifically on a challenge to the utility of the claimed compounds and the amount of experimentation necessary to use the compounds. In his answer to the applicants' appeal brief, the examiner stated that the final rejection was based on 35 U.S.C. § 112, paragraph 1.

The CAFC pointed out that Brana taught that his compounds were antitumor agents, and that the purpose of treating cancer with chemical compounds does not suggest an inherently unbelievable undertaking or involve implausible scientific principles. In re Jolles, 628 F.2d at 1327, 206 U.S.P.Q. at 890. The court also noted that modern science has previously identified numerous successful chemotherapeutic agents. As such, Brana's claimed method of treating cancer was not an incredible utility and did not require undue experimentation for one skilled in the art to practice.

The facts of the instant case are in accord with the CAFC's holding in In re Brana. In the instant case, Applicants have taught how to make the GSK-3 inhibitor compounds of Formula I. Applicants have further shown that the compounds are GSK-3 inhibitors and have provided enabling disclosure of routes of administration, pharmaceutical dosage forms and dosages in the claimed methods of treatment. Applicants respectfully submit that one skilled in the art would readily be able to make the instant compounds, compositions and practice the claimed methods of treatment without undue experimentation. The CAFC, in Genentech, Inc. v. Novo Nordisk A/S, 108 F.3d 1361, 42 U.S.P.Q.2d 1001 (Fed. Cir. 1997)offered the following guidance on enablement determinations in quoting Brenner v. Manson that "a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion. 383 U.S. 519, 536 (1966)." In the he art without undue experimentation. Applicants respectfully request that the Examiner consider claims 1-5 in view of these remarks and withdraw the 35 U.S.C. §112, first paragraph rejection.

The 35 U.S.C. §112, second paragraph rejection

Claims 1-5 have been rejected as allegedly being indefinite. Specifically, the Examiner stated that the numbering of the substituents in the definition of R1 and R2 is indefinite because the group numbering begins with (ii) rather than (i). Applicants have

corrected this numbering in the preceding amendment to the claims. Applicants respectfully submit that the claims, as amended, are clear, definite and distinctly claim the subject matter. Applicants respectfully request the Examiner to reconsider the claims as amended and withdraw the 35 U.S.C. 112, second paragraph rejection.

Having addressed all points and concerns raised by the Examiner, Applicants respectfully submit that the claims are in condition for allowance. An early and favorable action in this application is respectfully requested.

Respectfully submitted,

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